Robertson or O'Daly and Callan or Weiser. The Examiner's grounds for rejection are hereinafter traversed, and reconsideration is respectfully requested.

It is respectfully submitted that none of the cited references teach or suggest adjusting the volumetric ratio of lysing agent to blood in correspondence with an operator input indicative of the species of the blood as defined in each of independent claims 27, 35, 38 and 40.

As has been established, Yamamoto shows an automatic blood analyzer but fails to teach or suggest an apparatus comprising a control unit or like means for adjusting the volumetric ratio of lysing agent to blood in correspondence with an operator input indicative of the species of the blood. Rather, as recognized by the Examiner, Yamamoto discloses a system that is fixed to make the same dilution ratios, with the same volumes of reagent-mixture components for every blood sample.

Kabata likewise does not teach or suggest adjusting or modifying the volumetric ratio of lysing agent to blood to correspond to an operator input and species, as recited in independent claims 27, 35, 38 and 40. Kabata's suggestion to adapt the commercially-available software for human blood so that it may be better used for research purposes in connection with animal blood concerns changing the histogram thresholds to accommodate animal (rabbit), as opposed to human cell types. The thresholds divide the cell populations on the histograms, and they cannot be changed on the systems identified (see, for example, Figure 2 of Kabata showing the thresholds in solid lines). Accordingly, Kabata suggests that the software might be adapted for research purposes to adjust the histogram thresholds to better accommodate the animal cell types tested. The "Technicon H1" software identified by Kabata similarly modified the histogram thresholds for rats and dogs, but did not require different reagent mixtures for the different species.

Accordingly, Kabata makes no teaching or suggestion of adjusting or creating different reagent mixtures in response to different operator inputs, much less adjusting the volumetric ratio of lysing agent to blood to correspond to any one of a plurality of different operator inputs and respective species, as recited in independent claims 27, 35, 38 and 40. Thus, Kabata does not teach or suggest modification of Yamamoto to achieve the claimed invention.

Taylor discusses various staining techniques for flow cytometry, but does not suggest adjusting or creating different reagent mixtures. Accordingly, Taylor does not materially add to the teachings of Yamamoto and Kabata with respect to the present invention.

Callen is not prior art with respect to the present invention. Callen was published in October 1992, less than one year prior to the effective filing date of the present application (January 21, 1993). In any event, and without admitting that Callen is prior art with respect to the present invention, Callen shows evaluation of a system for hemoglobin measurement in dogs, cats, horses, and cows. Although Callen summarizes test result range differentials between those species, Callen does not suggest alteration of the testing process for different species. Thus, Callen does not teach or suggest changing the ratio of lysing agent to blood for different species, but rather effectively teaches away from doing so by showing acceptable results obtained without regard to species during the actual testing. Therefore, even if Callen were prior art with respect to the present invention, which it is not, it would not materially add to the teachings of Yamamoto, Kabata, and Taylor with respect to the present invention.

Weiser discusses various hematological techniques for different species, but does not suggest adjusting or creating different reagent mixtures. Weiser shows alteration of a device aperture current in order to count particles of sizes specific to common veterinary subjects. Weiser also shows doubling the dilution ratio where the particles are too numerous to be counted accurately by the subject device. Weiser does not make any suggestion to adjust the volumetric ratio of lysing agent to blood according to the subject species. Accordingly, Weiser does not materially add to the teachings of Yamamoto, Kabata, Taylor, and Callen with respect to the present invention.

Dixon shows experimental results derived from tests using non-standard concentrations of the lysing agent Zapoglobin on canine leukocytes. In sum, Dixon concludes that adjusting the volume of the lytic agent has no significant effect, but rather increasing the time of exposure to the standard concentration of the lytic agent did significantly increase lysis. Specifically, Dixon states in the abstract on page 249: "Canine leukocytes did not show significantly increased lysis when

subjected to Zapoglobin at approximately four times the standard concentration, but did do so on exposure to the standard concentration for longer than five minutes". See also FIG. 2 on page 251 where the effect of high and low concentrations of Zapoglobin on leukocyte counts are compared reflecting virtually no difference.

Accordingly, Dixon specifically teaches that changing the standard concentration of lytic agent has no significant effect on increasing lysis, and therefore Dixon, in effect, teaches away from adjusting the volume of lyse to blood in response to different operator inputs indicative of different species, as recited in the independent claims. Rather, if anything, Dixon might suggest that one could change the exposure time to the standard concentration of the lytic agent in order to increase or decrease lysis. The paragraph cited by the Examiner at page 252 of Dixon similarly in no way teaches or suggests the present invention as recited in the independent claims. Rather, this paragraph merely reiterates the conclusions set forth in the abstract on page 249.

The non-obvious nature of the present invention over Dixon is further evidenced by the more than 10 year period between the publishing of the Dixon reference and the filing of the present application. Although Dixon taught that there was no concentration dependent effect for the Zapoglobin lysing agent on canine leukocytes, a commercial embodiment of the present invention does accurately analyze canine leukocytes via automatic adjustment of lysing agent mixtures upon the pressing of a button corresponding to the canine species, in spite of the contrary teachings of Dixon. Thus, it would not have been obvious for one of average skill in the pertinent art to apply the teachings of Dixon in order to derive the present invention.

Halliday et al. and Robertson et al. do not materially add to the teachings of the other cited references with respect to the presently claimed invention. Halliday et al. do not teach or suggest in any way adjusting the ratio of lyse to blood on a species-by-species basis, as recited in the independent claims. Rather, Halliday et al. teach using the same ratio as prescribed by the "standard Coulter Counter technique". The only difference to the standard Coulter Counter

technique suggested by Halliday et al. was to change the order in which the components were mixed. (See Halliday et al. at 354).

The Examiner points out that Halliday et al. state at the end of the paper that similar variations have been found in "isolated specimens" of sheep and cat blood. However, this does not in any way teach or suggest the claimed invention. Rather, Halliday et al. make no teaching or suggestion as to what the cause of this variation might be. Further, Halliday et al.'s statement that the variation occurred only in "isolated specimens" would reasonably lead one of ordinary skill in the pertinent art to simply believe that the standard Coulter Counter technique is acceptable for most sheep and cats. Again, Halliday et al. make no teaching or suggestion of adjusting the volumetric ratio of lyse to blood on a species-by-species basis as recited in the present claims.

Robertson et al. do not relate in any way to automated hematology analyzers, much less such analyzers that adjust the ratio of lyse to blood on a species-by-species basis, as recited in the present claims. Rather, Robertson et al.'s paper is directed solely to modified staining techniques for avian blood cells. Although the Examiner correctly points out that Robertson et al. mention the prior development of a diluent then used widely by avian hematologists, there is no description of the diluent, much less any teaching or suggestion of modifying the lyse/diluent ratio, as suggested by the Examiner.

In sum, Halliday et al. and Robinson et al. do not in any reasonably clear or precise way show that there is a species dependent response to the ratio of lyse to blood, much less teach or suggest modifying any of the other references of record to create analyzers that adjust the ratio of lyse to blood on a species-by-species basis, as recited in independent claims 27, 35, 38 and 40.

The newly cited O'Daly reference does not materially add to the teachings of Halliday et al. and Robinson et al., or any of the other cited references, with respect to the presently claimed invention. O'Daly is directed to explaining how the identified parasites penetrate the host cells,

and particularly vertebrae cells. (See the "Introduction" at page 222 and the "Discussion" at pages 229 and 230). For example, O'Daly concludes at page 229 that "All parasite strains presented the same phenomenon, however, the vertebrate cells' extracts showed no hemolytic activity. This suggests that disruption of cell membranes by trypanosomal extracts might be the biochemical explanation that enables the parasite to penetrate host cells." Clearly, O'Daly is directed to determined the biochemical explanation for that enables the parasites to penetrate the host cells.

Contrary to the Examiner's assertion, O'Daly, like the other cited references, does not suggest in any clear or precise way adjusting the ratio of lyse to blood on a species-by-species basis, much less the other features of the present invention as recited in the independent claims. Moreover, it is respectfully submitted that the Examiner's statement at page 5 of the Action that "figure 3 shows a concentration dependent effect on lysis properties", is not correct. Rather, at most, FIG. 3 of O'Daly shows the change in "per cent hemolysis" verses time. FIG. 3 makes no suggestion to change the concentration of either lyse or blood, much less adjusting such concentration on a species-by-species basis, as recited in the independent claims. Similarly, FIG. 4 and the accompanying explanation on page 226 of O'Daly do not in any way suggest adjusting the ratio of lyse to blood on a species-by-species basis, but rather simply indicate that normal red blood cells of several mammalian species had different sensitivities to the same lytic agent.

Applicant respectfully submits that it is only through impermissible hindsight reconstruction that one might conclude that O'Daly and the other cited references teach or suggest adjusting the ratio of lyse to blood on a species-by-species basis, as recited in the independent claims. The vague and ambiguous references in the prior art cited by the Examiner in no way teach or suggest the explicit features of the present invention as recited in the independent claims.

Accordingly, it is respectfully submitted that independent claims 27, 35, 38 and 40 are unobvious over the cited references for at least these reasons. It is further submitted that the

dependent claims are likewise unobvious over the cited references for at least the same reasons as the independent claims, and for reciting additional patentable subject matter.

Any additional fees or overpayments, other than those already paid, as a result of filing the present paper may be applied to Deposit Account No. 50-1631. It is respectfully submitted that claims 27-30, 32-35, and 38-45, and an early action to that effect is earnestly solicited.

If after reviewing this Response, the Examiner believes that a telephone interview would facilitate the resolution of any remaining matters, or if the Examiner has any questions or requires any further information, the Examiner is requested to call the undersigned at the telephone number below.

Respectfully submitted,

Date: February 11, 2002

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